

### **REMARKS**

The Office Action of September 24, 2007, presents the examination of claims 1-4, 12-14, 18-24, 28, 34-36 and 46-48, the remaining being withdrawn pursuant to a Restriction Requirement.

#### **A housekeeping matter**

The present paper is accompanied by a Power of Attorney and Change of Correspondence Address, shifting correspondence in this matter to the firm of Birch, Stewart, Kolasch & Birch, LLP. The Examiner's cooperation in ensuring that further correspondence is sent to BSKB would be appreciated.

#### **Amendments to the claims**

Claim 1 is presently amended to incorporate the recitations of claim 2. Claims 2 and 3 are accordingly canceled. The corresponding claims 34, 49-51, 53 and 54 are also canceled.

#### **Restriction requirement**

Claims 5-11, 15-17, 25-27, 32-33, 37-45 and 52 and 55-65 stand withdrawn pursuant to restriction. The claims as currently amended all recite as a feature of the invention a polynucleotide that encodes the genome or antigenome of a chimeric RSV, including human and bovine or mouse RSV nucleic acid sequences, that further includes one or more mutations from among the group of mutations included in a set of mutant RSV. In the instances of claims to the virus embodiments, the polynucleotide is the genome or antigenome of the virus. Applicants submit that the claims thus represent a unitary invention within the presently elected restriction group and that there is no undue burden of search imposed by examination of all of the presently pending claims, and therefore the instant restriction requirement should be withdrawn.

Pending method claims all are commensurate in scope with these composition claims, and Applicants submit that they could thus be rejoined upon a finding of allowability of the composition claims. MPEP § 821.04.

The Examiner did not respond to Applicants' argument on this point in the Final Office Action, and so Applicants request that the status of the restriction requirement be clarified in the next communication from the Office.

Rejections over prior art

Claims 1, 4, 12, 18, 21-24, 35, 36 and 46-48 stand rejected under 35 USC § 103(a) as being unpatentable over Clarke '520 in view of Collins (PNAS vol. 92) and further in view of Murphy '326. This rejection is traversed. Reconsideration and withdrawal thereof are respectfully requested.

Applicants submit that the Examiner fails to establish *prima facie* obviousness of the present invention. In particular, the Examiner is using impermissible hindsight to assemble the present invention from elements of the prior art, using the Applicants disclosure as a template. Such an approach to asserting a case of *prima facie* obviousness is improper and cannot be sustained. See, e.g. *In re Fritch*, 23 USPQ2d 1780 (Fed. Cir. 1992). Furthermore, an expectation of success in accomplishing the modification suggested by the Examiner must be present at the time the invention was made. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

Murphy '326 is cited for disclosure of the particular mutant strains recited in claim 13. However, Murphy '326 does not disclose the nucleotide sequence of any of the mutant viruses, and in particular does not provide any description of the particular changes in nucleotide sequence that are to be made in order to introduce the various attenuating point mutations harbored by, for example RSV cpts 248, into a different virus, i.e. one having a chimeric genome or antigenome. That information is critical to implementing the invention of the present application and is provided by the present specification.

Neither Clarke '520 nor Collins (PNAS vol. 92) supply this information. Thus, the combined references cited by the Examiner do not disclose or suggest the present invention and so the instant rejection fails and must be withdrawn.

The Examiner's reasons for maintaining the rejection in the first instance relate to an idea that, given alleged teachings of Clark '520 that one can insert or replace portions of one RSV genome with portions of another, one could simply insert the heterologous genome segments

desired into the existing viruses of Murphy '326 that include the various mutations described in that patent to obtain the instantly claimed invention. Therefore, the Examiner alleges, Applicants' argument is not persuasive because the precise sequence of the point mutations in the panel of viruses recited in the instant claim 1 need not be known.

This argument is spurious in the first instance, as without knowledge of the particular sequence and location of a mutation, one of skill in the art could not have any reasonable expectation of success in moving a sequence from the bovine or mouse RSV genome into the human RSV genome including the point mutation with retention of the attenuation phenotype. That is, upon moving the heterologous sequence into the human RSV genome, the attenuating mutation may be taken out by the replacement process. Alternatively, the mutation could well abolish a restriction site that is required for the moving process, or generate a new one that would result in failure to properly reassemble the recombinant viral genome.

The Examiner does acknowledge that his argument does not apply to the previously amended claim 2, and thus should not apply to the presently amended claim 1, which incorporates the features of claim 2, now canceled.

Claims 1, 2, 4, 12, 18, 21-24, 34-36 and 46-48 are rejected under 35 USC § 103(a) as being unpatentable over Clarke and Collins as applied above, in further view of Wertz. This rejection is traversed. Reconsideration and withdrawal thereof are requested.

Applicants submit that the Examiner fails to establish *prima facie* obviousness of the invention as claimed for the reasons explained above. The Examiner has in this instance acknowledged that Applicants' previous arguments for patentability were persuasive as to amended claim 3, as he has removed this claim from the rejection (see paragraph 11 of the Final Office Action at page 5). Applicants are not certain why claim 2 would not also be removed from this rejection, as certainly human-bovine chimeras are as distinct from the references as human-human chimeras are.

More to the point, Wertz '229 does not at all describe any sort of functional recombinant RSV genome or antigenome that provides a replicating viral particle. Rather, Wertz '229 describes expression of RSV proteins from "minigenome" plasmids comprising a 3' leader and

5' trailer of RSV and having deletion of most of the "internal" genes of the virus. The replication of the minigenome plasmids having a mutation in the trailer region ("panhandle") or wild-type trailer region was assessed in the presence of plasmids expressing the N, P and L proteins of RSV. By such an experiment, Wertz determined that a sequence in the trailer region and the L protein are both necessary for efficient replication of the RSV genome.

Thus, Wertz '229 adds nothing to the combination of Clarke, Collins and Murphy that cures the deficiencies of the combination of these references in failing to render obvious the presently-claimed invention.

#### Obviousness-type double patenting rejections

The Examiner has pronounced a "new warning" about double patenting related to identity of claims 3 and 34. Both of these claims are canceled, rendering the new warning moot.

Claims 1, 4, 12, 14, 18-24, 28, 35 and 46-48 remain rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-4, 12, 14, 18, 20-25, 28 and 31-34 of US Patent 6,689,367.

Applicants reiterate that the subject matter of this application that is deemed obvious over the claims of the 6,689,367 patent was restricted from the application that became that patent and so a double-patenting rejection is improper in this instance. Applicants provide attached hereto a copy of the restriction requirement made during prosecution of the '367 patent. The Examiner should take due note that the patented subject matter in the '367 patent relates to Group I, whereas the subject matter of the present application is in Group X.

As the USPTO has already made a determination that the subject matter claimed in the '367 patent and the present subject matter are patentably distinct inventions, the instant rejection should be withdrawn.

#### CONCLUSION

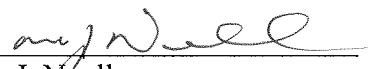
In view of the above amendments and remarks, Applicants submit that the present claims are allowable.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: October 24, 2008

Respectfully submitted,

By   
Mark J. Nuell  
Registration No.: 36,623  
BIRCH, STEWART, KOLASCH & BIRCH, LLP  
12770 High Bluff Drive  
Suite 260  
San Diego, California 92130  
(858) 792-8855  
Attorney for Applicants